FunClust: Identification of functional motifs in non homologous proteins using multiple local structure comparison.

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Motivation

Functional motifs in protein structures, such as active sites or ligand binding sites, can be identified using local structural comparison methods. These methods can be based on two alternative strategies: by searching a library of motif templates on a structure of unknown function or by searching similarities between two protein structures which are known or expected to share the same function. The first approach is more robust, but requires the manual construction of functional site templates, which are difficult to build and validate. In addition, it cannot be applied to ligand binding sites or protein-protein interfaces, because they are less amenable to be described by templates. The problem with the second approach lies in the validation of the identified similarities. This issue can be partially solved by performing a multiple structural comparison of more than two proteins sharing the same functional motif.

Methods

Results

We developed FunClust a new multiple structural alignment web server that uses a local (as opposed to global) structural comparison program, and therefore can be used to identify short structural motifs irrespective of the order in which the residues appear in the primary sequence. The server can be used to identify conserved functional motifs in a set of non homologous protein structures. Users can submit a set of protein structures deemed to share a common function (e. g. they bind similar ligands, interact with similar protein interfaces or share an enzymatic activity).

The server finds and lists structural motifs composed by three or more spatially well conserved residues shared by at least three of the submitted structures. FunClust uses a local structural comparison algorithm to identify subsets of similar amino acids between each pair of input protein chains and a clustering procedure to group the similarities shared between different structure pairs. The method is fast, completely sequence independent, and does not need an a priori knowledge of the motif to be found. The final output is a list of aligned structural matches displayed in both tabular and graphical form.

Availability: http://pdbfun.uniroma2.it/funclust

Image: http://pdbfun.uniroma2.it/funclust/Figure1.jpg

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